

**Amendments to the Claims:**

This listing of the claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

1-143 (Cancelled)

144 (Currently Amended). A method of identifying and producing a peptide that interacts with a ligand that interacts with a discontinuous epitope of a single biological unit consisting of a single protein, or consisting of two or more proteins that interact to form a complex, the method comprising:

- (a) providing a plurality of DNA fragments consisting of fragments, each of which appears in a DNA sequence that encodes the single biological unit;
- (b) creating a library consisting of oligonucleotides from said plurality of DNA fragments, each said oligonucleotide comprising at least two contiguous ~~of said~~ fragments, said fragments being randomly ligated such that any oligonucleotide in the library can ligate with any other oligonucleotide in the library;

- (c) inserting each of said oligonucleotides from said library of oligonucleotides into an expression system;
- (d) causing the peptides encoded by said oligonucleotides to be expressed;
- (e) screening the expressed peptides for interaction with a ligand that interacts with a discontinuous epitope of said single biological unit;
- (f) identifying any peptide which so interacts; and
- (g) producing any peptide so identified.

145 (Previously Presented). A method in accordance with claim 144, wherein said procedure of (a) comprises cutting said DNA sequence to form said plurality of DNA fragments.

146-148 (Cancelled)

149 (Previously Presented). A method in accordance with claim 144, wherein said procedure of (b) comprises randomly ligating said plurality of DNA fragments to one another to form at least one ligated fragment and at least partially digesting said at least one ligated fragment to form said library of oligonucleotides.

150-158 (Cancelled).

159 (Currently Amended). A method of preparing a library of peptides that can be screened to find peptides that interact with ligands that interact with discontinuous epitopes of a single biological unit consisting of a single protein, or consisting of two or more proteins that interact to form a complex, comprising:

- (a) providing a plurality of DNA fragments consisting of fragments, each of which appears in a DNA sequence that encodes the single biological unit;
- (b) creating a library consisting of oligonucleotides from said plurality of DNA fragments, each said oligonucleotide comprising at least two ~~of said~~ contiguous fragments, said fragments being randomly ligated such that any oligonucleotide in the library can ligate with any other oligonucleotide in the library;
- (c) inserting each of said oligonucleotides from said library of oligonucleotides into an expression system; and
- (d) causing the peptides encoded by said oligonucleotides to be expressed, thereby preparing a library of peptides.

160 (Previously Presented). A method in accordance with claim 159, wherein said procedure of (a) comprises cutting said DNA sequence to form said plurality of DNA fragments.

161-162 (Cancelled)

163 (Previously Presented). A method in accordance with claim 159, wherein said procedure of (b) comprises randomly ligating said plurality of DNA fragments to one another to form at least one ligated fragment and at least partially digesting said at least one ligated fragment to form said library of oligonucleotides.

164-176 (Cancelled).

177 (Previously Presented). A method in accordance with claim 144, wherein each of said DNA fragments of (a) has a size of about 50 to about 150 base pairs.

178 (Cancelled).

179 (Previously Presented). A method in accordance with claim 159, wherein each of said DNA fragments of (a) has a size of about 50 to about 150 base pairs.

180-183 (Cancelled).

184 (Currently Amended). A method of identifying and producing a peptide that interacts with a ligand that interacts with a discontinuous epitope of a single biological unit consisting of a single protein having a single definable

sequence, or consisting of two or more proteins, each having a single definable sequence, which proteins interact to form a complex, the method comprising:

- (a) providing a plurality of DNA fragments consisting of fragments, each of which appears in a DNA sequence that encodes the single biological unit;
- (b) creating a library consisting of oligonucleotides from said plurality of DNA fragments, each said oligonucleotide comprising at least two contiguous ~~of said~~ fragments, said fragments being randomly ligated;
- (c) inserting each of said oligonucleotides from said library of oligonucleotides into an expression system;
- (d) causing the peptides encoded by said oligonucleotides to be expressed;
- (e) screening the expressed peptides for interaction with a ligand that interacts with a discontinuous epitope of said single biological unit;
- (f) identifying any peptide which so interacts; and
- (g) producing any peptide so identified.

185 (Currently Amended). A method of preparing a library of peptides that can be screened to find peptides that interact with ligands that interact with discontinuous epitopes of a single biological unit consisting of a single protein having a single definable sequence, or consisting of two or more proteins, each having a single definable sequence, which proteins interact to form a complex, comprising:

- (a) providing a plurality of DNA fragments consisting of fragments, each of which appears in a DNA sequence that encodes the single biological unit;
- (b) creating a library consisting of oligonucleotides from said plurality of DNA fragments, each said oligonucleotide comprising at least two contiguous ~~of said~~ fragments, said fragments being randomly ligated;
- (c) inserting each of said oligonucleotides from said library of oligonucleotides into an expression system; and
- (d) causing the peptides encoded by said oligonucleotides to be expressed, thereby preparing a library of peptides.

186-190 (Cancelled)

191 (Currently Amended). A method in accordance with claim 144, wherein said single biological unit consists of a single protein having a single definable sequence, or consists of two or more proteins, each having a single definable sequence, which proteins interact to form a complex.

192 (Currently Amended). A method in accordance with claim 159, wherein said single biological unit consists of a single protein having a single definable sequence, or consists of two or more proteins, each having a single definable sequence, which proteins interact to form a complex.

193-194 (Cancelled)

195 (New). A method of identifying and producing a peptide which interacts with a ligand which interacts with a discontinuous epitope of a single biological unit consisting of a single protein or consisting of two or more proteins which interact to form a complex, the method comprising:

- (a) providing a plurality of DNA fragments consisting of fragments, each of which appears in a DNA sequence that encodes the single biological unit;
- (b) creating a library consisting of oligonucleotides from said plurality of DNA fragments, each said oligonucleotide comprising

at least two contiguous fragments, said  
fragments being randomly ligated ;

- (c) inserting each of said oligonucleotides from  
said library of oligonucleotides into an  
expression system;
- (d) causing the peptides encoded by said  
oligonucleotides to be expressed;
- (e) screening the expressed peptides for  
interaction with a ligand that interacts with a  
discontinuous epitope of said single biological  
unit;
- (f) identifying any peptide which so interacts; and
- (g) producing any peptide so identified.

196 (New). A method in accordance with claim 195,  
wherein said procedure of (a) comprises cutting said DNA  
sequence to form said plurality of DNA fragments.

197 (New). A method in accordance with claim 196,  
wherein said cutting is accomplished enzymatically.

198 (New). A method in accordance with claim 196,  
wherein said cutting is accomplished mechanically.

199 (New). A method in accordance with claim 195,  
wherein said procedure of (a) comprises synthesizing said  
plurality of DNA fragments.



200 (New). A method in accordance with claim 195, wherein said procedure of (b) comprises randomly ligating said plurality of DNA fragments to form at least one ligated fragment and at least partially digesting said at least one ligated fragment to form said library of oligonucleotides.

201 (New). A method in accordance with claim 195, wherein said expression system comprises a plurality of bacteria and said procedure of (c) comprises inserting one of said library of oligonucleotides into each of said plurality of bacteria.

202 (New). A method in accordance with claim 195, wherein said expression system comprises a plurality of phages and said procedure of (c) comprises inserting one of said library of oligonucleotides into each of said plurality of phages.

203 (New). A method in accordance with claim 202, wherein said oligonucleotides are inserted into said phages by cloning said oligonucleotides into phage genes coding for a coat protein.

204 (New). A method in accordance with claim 203, wherein said phages are filamentous phages and said coat protein is pIII or pVIII.

205 (New). A method in accordance with claim 195, wherein said expression system comprises a eukaryotic

expression system and said procedure of (c) comprises inserting said library of oligonucleotides into eukaryotic expression vectors and inserting said vectors into said eukaryotic expression system.

206 (New). A method in accordance with claim 195, wherein said single biological unit is a single protein.

207 (New). A method in accordance with claim 195, wherein said single biological unit is two or more proteins which interact to form a complex.

208 (New). A method in accordance with claim 195, wherein each of said DNA fragments of (a) has a size of about 50 to about 150 base pairs.

209 (New). A method of preparing a library of peptides which can be screened to find peptides that interact with ligands which interact with discontinuous epitopes of a single biological unit consisting of a single protein or consisting of two or more proteins which interact to form a complex, comprising:

- (a) providing a plurality of DNA fragments consisting of fragments, each of which appears in a DNA sequence that encodes the single biological unit;
- (b) creating a library consisting of oligonucleotides from said plurality of DNA

fragments, each said oligonucleotide comprising  
at least two contiguous fragments, said  
fragments being randomly ligated ;

(c) inserting each of said oligonucleotides from  
said library of oligonucleotides into an  
expression system; and

(d) causing the peptides encoded by said  
oligonucleotides to be expressed, thereby  
preparing a library of peptides.

210 (New). A method in accordance with claim 209,  
wherein said procedure of (a) comprises cutting said DNA  
sequence to form said plurality of DNA fragments.

211 (New). A method in accordance with claim 210,  
wherein said cutting is accomplished enzymatically.

212 (New). A method in accordance with claim 210,  
wherein said cutting is accomplished mechanically.

213 (New). A method in accordance with claim 209,  
wherein said procedure of (b) comprises randomly ligating said  
plurality of DNA fragments to form at least one ligated  
fragment and at least partially digesting said at least one  
ligated fragment to form said library of oligonucleotides.

214 (New). A method in accordance with claim 209,  
wherein said expression system comprises a plurality of  
bacteria and said procedure of (c) comprises inserting one of

said library of oligonucleotides into each of said plurality of bacteria.

215 (New). A method in accordance with claim 209, wherein said expression system comprises a plurality of phages and said procedure of (c) comprises inserting one of said library of oligonucleotides into each of said plurality of phages.

216 (New). A method in accordance with claim 215, wherein said oligonucleotides are inserted into said phages by cloning said oligonucleotides into phage genes coding for a coat protein.

217 (New). A method in accordance with claim 216, wherein said phages are filamentous phages and said coat protein is pIII or pVIII.

218 (New). A method in accordance with claim 209, wherein said expression system comprises a eukaryotic expression system and said procedure of (c) comprises inserting said library of oligonucleotides into eukaryotic expression vectors and inserting said vectors into said eukaryotic expression system.

219 (New). A method in accordance with claim 209, wherein said single biological unit is a single protein.

Appln. No. 09/297,668

Amdt. dated February 10, 2005

Reply to Office action of August 10, 2004

220 (New). A method in accordance with claim 209, wherein said single biological unit is two or more proteins which interact to form a complex.

221 (New). A method in accordance with claim 209, wherein each of said DNA fragments of (a) has a size of about 50 to about 150 base pairs.